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(FILE 'HOME' ENTERED AT 17:03:04 ON 26 MAY 2003)

FILE 'MEDLINE, BIOSIS' ENTERED AT 17:03:44 ON 26 MAY 2003

L1 131966 S OEDEMA OR EDEMA
L2 139921 S TNF OR (TNF (W) ALPHA) OR (TUMOR (W) NECROSIS (W) FACTOR) OR
L3 0 S (SER100 (3A) GLU116) OR (SER99 (3A) GLU115)
L4 0 S (SER100 (S) GLU116) OR (SER99 (S) GLU115)
L5 653 S L1(S) L2
L6 270 S L5 (S) (LUNG OR PULMONARY)
L7 4 S L6 (S) (PEPTIDE OR FRAGMENT)
L8 4 DUP REM L7 (0 DUPLICATES REMOVED)

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L6 ANSWER 13 OF 270 MEDLINE

TI Mechanisms of TNF-alpha stimulation of amiloride-sensitive sodium transport across alveolar epithelium.

AU Fukuda N; Jayr C; Lazrak A; Wang Y; Lucas R; Matalon S; Matthay M A
SO AMERICAN JOURNAL OF PHYSIOLOGY. LUNG CELLULAR AND MOLECULAR PHYSIOLOGY, (2001 Jun) 280 (6) L1258-65.

Journal code: 100901229. ISSN: 1040-0605.

AB . . . triple-mutant TNF-alpha or after preincubation with blocking antibodies to the two TNF-alpha receptors before perfusion with TNF-alpha. In conclusion, although **TNF- alpha** can initiate acute inflammation and **edema** formation in the lung, **TNF-alpha** can also increase AFC by an amiloride-sensitive, cAMP-independent mechanism that enhances the resolution of alveolar **edema** in pathological conditions by either binding to its receptors or activating Na(+) channels by means of its lectinlike domain.

AB Because tumor necrosis factor (TNF)-alpha can upregulate alveolar fluid clearance (AFC) in pneumonia or septic peritonitis, the mechanisms responsible for the TNF-alpha-mediated increase in epithelial fluid transport were studied. In rats, 5 microg of TNF-alpha in the alveolar instillate increased AFC by 67%. This increase was inhibited by amiloride but not by propranolol. We also tested a triple-mutant TNF-alpha that is deficient in the lectinlike tip portion of the molecule responsible for its membrane conductance effect; the mutant also has decreased binding affinity to both TNF-alpha receptors. The triple-mutant TNF-alpha did not increase AFC. Perfusion of human A549 cells, patched in the whole cell mode, with TNF-alpha (120 ng/ml) resulted in a sustained increase in Na(+) currents from 82 +/- 9 to 549 +/- 146 pA (P < 0.005; n = 6). The TNF-alpha-elicited Na(+) current was inhibited by amiloride, and there was no change when A549 cells were perfused with the triple-mutant TNF-alpha or after preincubation with blocking antibodies to the two TNF-alpha receptors before perfusion with TNF-alpha. In conclusion, although **TNF- alpha** can initiate acute inflammation and **edema** formation in the lung, **TNF-alpha** can also increase AFC by an amiloride-sensitive, cAMP-independent mechanism that enhances the resolution of alveolar **edema** in pathological conditions by either binding to its receptors or activating Na(+) channels by means of its lectinlike domain.

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- L8 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
- TI Beneficial effects of a **tumor necrosis factor**
-derived **peptide** in an ex vivo isolated perfused rat
lung model of alveolar **edema**.
- AU Lucas, R. (1); Elia, N.; Braun, C. (1); Fransen, L.; Hamacher, J. (1);
Morel, D.; Wendel, A. (1)
- SO Naunyn-Schmiedeberg's Archives of Pharmacology, (2001) Vol. 363, No. 4
Supplement , pp. R111. print.
Meeting Info.: 42nd Spring Meeting of the German Society for Experimental
and Clinical Pharmacology and Toxicology Mainz, Germany March 13-15, 2001
ISSN: 0028-1298.
- TI Beneficial effects of a **tumor necrosis factor**
-derived **peptide** in an ex vivo isolated perfused rat
lung model of alveolar **edema**.

	Type	L #	Hits	Search Text	DBs	Time Stamp
1	BRS	L1	2	"5891679"	USPAT; US-PGP UB	2003/05/26 16:40
2	BRS	L4	19354	(oedema or edema)	USPAT; US-PGP UB; EPO; JPO; DERWEN T	2003/05/26 16:42
3	BRS	L10	21708	TNF or (TNF adj alpha) or (tumor adj necrosis adj factor) or (tumor adj necrosis adj factor adj alpha)	USPAT; US-PGP UB; EPO; JPO; DERWEN T	2003/05/26 16:44
4	BRS	L16	1	(ser100 adj3 glu116) or (ser99 adj3 glu115)	USPAT; US-PGP UB; EPO; JPO; DERWEN T	2003/05/26 16:46
5	BRS	L22	228	L4 same L10	USPAT; US-PGP UB; EPO; JPO; DERWEN T	2003/05/26 16:47